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Prevalence of Symptoms of Benign Prostatic Hyperplasia in Umudike and its Relationship with Measures of Obesity

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ABSTRACT

Benign prostate hyperplasia is one of the major health challenges of older men and is thought to be linked to obesity. This study investigated the prevalence of clinical symptoms of BPH in 747 male Nigerians aged 40 years or older and assessed the relationship between the symptom scores and measures of obesity. The International Prostate Symptom Score (IPSS) was used to diagnose the clinical symptoms of BPH. Anthropometric data were collected using standard protocol and Body Mass Index (BMI), Waist-to-Hip Ratio (WHpR) and Waist-to-Height Ratio (WHtR) were derived. Appropriate statistical tools were used for the data analysis. The prevalence of BPH (moderate-to-severe symptoms) in the studied population is 35.3% (6.0% in those aged 40-49 years to 69.9% in those aged 70+ years). Compared to those with mild symptoms of BPH, BMI and WHtR did not differ significantly ($p > 0.05$) (though WHpR was significantly higher ($p < 0.05$)) in those with either moderate or severe symptoms. Only WHpR was found to be minimally associated with symptoms of BPH. The prevalence of symptoms of BPH is very high in this population and it appears that visceral adiposity may be the critical part of obesity that is related to BPH.

Key words: Benign prostatic hyperplasia, obesity, prevalence, relationship

INTRODUCTION

The prostate gland is walnut-sized in young post-pubertal men, but gradually enlarges from about the fourth decade of life due to a variety of factors. Though prostate cancer, Benign Prostatic Hyperplasia (BPH) and prostatitis are known to afflict the prostate, BPH is the most common urologic disease suffered by elderly men and one of the most common chronic diseases of males (Ejike and Eeanyika, 2008; Parsons *et al.*, 2013). It affects an estimated one-in-four men in their 50s, one-in-three men in their 60s and one-in-two men in their 80s (Kramer *et al.*, 2007; Robert *et al.*, 2009). At autopsy, the histological prevalence of BPH is 50% in men aged 50-60 years and 90% in men older than 80 years (Patel and Parsons, 2014). In Nigeria, it has been reported that one-in-four men older than 40 years have symptoms suggestive of BPH (Ezeanyika *et al.*, 2006). If untreated, BPH may progressively result in bladder dysfunction and eventually lead to acute urinary retention, sepsis, toxemia and ultimately death (Roehrborn *et al.*, 2008).

The pathogenesis of BPH is still not elucidated completely. It is (like most chronic diseases) progressive, requiring a long period to evolve from prostatic tissue alterations to the onset of Lower Urinary Tract Symptoms (LUTS), the clinical expression of BPH (Fitzpatrick, 2006). Senescence in epithelial cells is thought to result in abnormal cellular response to signalling molecules and

growth factors, leading to the development of the epithelial hyperplasia seen in BPH. Furthermore, increase in stromal volume observed in BPH is explained by the observation that hyperplastic nodules are characterized by a reduced epithelium-to-stroma ratio, relative to normal prostate tissue, which arises due to an age-related imbalance between growth and apoptosis in stromal cells (Claus *et al.*, 1997).

Besides age, imbalances in steroid hormones metabolism are important factors in the pathogenesis of BPH. Testosterone and its (5α-reductase type II-reduced) metabolite dihydrotestosterone (DHT) promote growth and differentiation of prostate cells by (upon binding to the androgen receptor) inducing the synthesis of growth factors (within the stroma), that act on the prostatic epithelia and stroma (Roehrborn *et al.*, 2008). Oestrogens have also been reported to stimulate the prostate tissue growth subsequent to the age-related decline in the testosterone: oestrogens ratio. This growth reactivation (after a period of post-pubertal quiescence) leads to a preferential proliferation of stromal cells of the prostate (Kawashima and Nakatani, 2012) and the attendant BPH.

Without prejudice to the above classical causal BPH patho-etiologic paradigms, current scientific thought suggests that systemic metabolic disturbances may also contribute significantly to the pathogenesis of BPH (Ejike, 2014; Rees and Kirby, 2014). It is currently thought that obesity promotes BPH and that inflammation is at the centre of that association. This position is supported by many large studies (Parsons *et al.*, 2013; Kristal *et al.*, 2007), such that BPH has been suggested to be a component of the metabolic syndrome (Ejike and Ezeanyika, 2008).

Quantifying those with BPH and understanding the relationships between BPH and modifiable lifestyle factors are central to distributing scarce resources for BPH management and developing appropriate prevention strategies. Therefore, this study investigated the prevalence of symptoms of BPH in Umudike, a University town in Abia State, South-East Nigeria and assessed the relationship between BPH symptom scores and different measures of obesity.

MATERIALS AND METHODS

Subjects: Adult male members of staff of Michael Okpara University of Agriculture and National Root Crops Research Institute, both in Umudike, Abia State, Nigeria (aged 40 years and older) were individually approached to participate in this random cross-sectional population-based study. The objectives of the study were explained to them and informed consent obtained from each willing participant. Exclusion criteria were illiteracy and overt morbidity from any disease. Seven hundred and forty seven adult males were ultimately recruited. The Helsinki declaration was followed strictly and the Board of the Department of Biochemistry, Michael Okpara University of Agriculture, Umudike, approved the design and protocol for this study. No honoraria were paid to the participants.

Methods: The International Prostate Symptom Score (IPSS) index, a modification of the American Urological Association (AUA) symptom index requires little skill and no laboratory equipment. It has been shown that it is valid for use in Nigeria for both diagnosis and management of BPH (Ezeanyika *et al.*, 2006; Amu *et al.*, 2013) and was therefore, used in this study to diagnose the clinical symptoms of BPH. Mild, moderate and severe symptoms of BPH were defined by a symptom score of 0-7, 8-19 and 20-35 points, respectively. Subjects with moderate-to-severe symptoms were regarded as having LUTS suggestive of BPH.

The heights of the subjects were measured using an inelastic measuring tape, fastened to a vertical rod, to the nearest 0.1 cm, with the subject standing on bare feet. Weights of subjects were measured using a digital display electronic scale (Sayona, Model: SYS-961), with the subjects in light clothing, to the nearest 0.1 kg. Waist circumferences and hip circumferences were measured around the umbilicus and the widest circumference around the buttocks, respectively, using an inelastic measuring tape, to the nearest 0.1 cm. All measurements were taken by the same trained personnel. From the anthropometric measurement taken, the subjects' Body Mass Index (BMI), Waist-to-Hip Ratio (WHpR) and Waist-to-Height Ratio (WHtR) were calculated using standard internationally accepted equations.

Statistics: Descriptive statistical analysis was carried out on the data generated and differences between means separated by one-way ANOVA. The relationships between the BPH symptom scores and the measures of obesity were assessed using Pearson's correlation coefficients and linear regression analysis. The correlation analysis was done for each age range separately and for the entire dataset. For all analyses, the significant threshold was fixed at $p \leq 0.05$. Data analyses were done using IBM-SPSS for windows, version 20 (IBM Corp., Atlanta, GA).

RESULTS

Of all the subjects studied, 28.9, 26.2, 23.0 and 21.8% belonged to the age ranges 40-49, 50-59, 60-69 and 70+ years, respectively. Severe symptoms of BPH were found in 5.0% of the general population. It increased linearly with age from 0.0% among those aged 40-49 years to 12.9% among those older than 69 years. Similarly, moderate symptoms were found in 30.4% of the general population and it also increased linearly with age from 6.0% (40-49 years) to 57.1% (70+ years). The prevalence of LUTS suggestive of BPH (moderate-to-severe symptoms) is therefore, 35.3% in the general population (6.0% in those aged 40-49 years to 69.9% in those aged 70+ years) (Table 1).

Compared to those with mild symptoms of BPH, BMI did not differ significantly ($p>0.05$) in those with either moderate or severe symptoms, in the general population or within any age range. Though subjects with severe symptoms of BPH had statistically similar ($p<0.05$) WHpR compared to those with mild symptoms, those with moderate symptoms had significantly higher ($p<0.05$) WHpR relative to their counterparts with mild symptoms, in the general population. No significant differences in WHpR were however observed between subjects with any of the symptoms when they were stratified along age range lines. Data for WHtR followed the trend for BMI. The WHtR of the subjects were statistically similar ($p<0.05$) between the three symptom score groups, both in the general population and within the different age ranges (Table 2). Similar trends were observed when the data for those with moderate and severe symptoms were grouped together (data not presented).

Table 1: Prevalence of clinical symptoms of benign prostatic hyperplasia in the studied population

	Prevalence							
	Mild		Moderate		Severe		LUT/BPH*	
Age range years	No.	%	No.	%	No.	%	No.	%
40-49 n = 216	203	94.0	13	6.0	0	0.0	13	6.0
50-59 n = 196	143	73.0	48	24.5	5	2.6	53	27.0
60-69 n = 172	88	51.2	73	42.4	11	6.4	84	48.8
70 and older n = 163	49	30.1	93	57.1	21	12.9	114	69.9
Total n = 747	483	64.7	227	30.4	37	5.0	264	35.3

*Moderate-to-severe symptoms, that is symptom scores≥8, LUT/BPH: Lower urinary tract/Benign prostatic hyperplasia

Table 2: Mean values of indices of obesity in the studied population, stratified by age and nature of symptoms

Age range (years)	BMI			WHpR			WHtR		
	Mild	Moderate	Severe	Mild	Moderate	Severe	Mild	Moderate	Severe
40-49	23.9±3.1	24.6±3.6 (0.489)	-	0.87±0.05	0.88±0.04 (0.226)	-	0.49±0.05	0.51±0.48 (0.323)	-
50-59	24.4±3.2	23.6±3.2 (0.114)	23.7±2.3 (0.645)	0.87±0.06	0.89±0.05 (0.089)	0.88±0.04 (0.786)	0.50±0.05	0.50±0.05 (0.980)	0.51±0.05 (0.816)
60-69	23.6±3.2	23.6±2.9 (0.963)	23.4±3.9 (0.877)	0.87±0.04	0.88±0.05 (0.726)	0.88±0.04 (0.732)	0.50±0.05	0.50±0.05 (0.860)	0.49±0.05 (0.557)
70+	23.7±3.7	24.1±3.4 (0.358)	24.5±2.8 (0.215)	0.88±0.05	0.88±0.05 (0.466)	0.88±0.04 (0.947)	0.51±0.06	0.50±0.05 (0.616)	0.50±0.04 (0.661)
Total	24.0±3.2	23.9±3.2 (0.636)	24.1±3.2 (0.876)	0.87±0.05	0.88±0.05 (0.020)	0.88±0.04 (0.189)	0.50±0.05	0.50±0.05 (0.333)	0.50±0.05 (0.832)

Comparisons are made with reference to the "mild" group

Table 3: Correlation and regression data on the subjects, irrespective of age

	International prostate symptom score				
	Pearson correlation			Linear regression*	
	r	p	β	t	p
BMI	+0.003	0.935	+0.023	+0.491	0.624
WHpR	+0.066	0.072	+0.099	+2.115	0.035
WHtR	+0.009	0.817	-0.063	-1.115	0.265

*Regression model accounts for only 0.2% of the data (adjusted R^2 = 0.002)

Within each age range, the only measure of obesity that was found to be significantly correlated (p<0.05) with prostate symptom scores was WHpR among those aged 40-49 years. The correlation was nonetheless weak and negative (r = -0.155). For the other age ranges and other measures of obesity, the correlations were not significant (p>0.05) (Fig. 1). Table 3 shows data from the correlation and regression analyses done. None of the measures of obesity was significantly (p>0.05) correlated with prostate symptom scores. Only WHpR was found to be significantly associated with prostate symptom scores. The same result was obtained when the data for those with moderate and severe symptoms were lumped together (data not presented). The regression models however accounted for only 0.2-0.5% of the data.

DISCUSSION

The prevalence of moderate-to-severe symptoms suggestive of BPH found in this population (35.3%) is higher than the 25.4% prevalence reported earlier by Ezeanyika *et al.* (2006) in Nsukka, a different part of South-East Nigeria, though the same diagnostic instrument was used. The linear increase in the prevalence of the symptoms with age is consistent with the earlier report and other reports on the prevalence of BPH. This is understandable since BPH is known to be age-related (Seim *et al.*, 2005; Chokkalingam *et al.*, 2012; Amu *et al.*, 2013; Parsons *et al.*, 2013). Chokkalingam *et al.* (2012) reported a prevalence of 19.9% for moderate-to-severe symptoms of BPH in Ghana and concluded that "BPH and/or LUTS appear to be quite common among older Ghanaian men". This study, just like the earlier mentioned study from Nigeria can be justifiably compared to ours since the same instrument was used to arrive at the prevalence values. Clearly therefore, the values reported in the current study are higher than earlier reports from Nigeria and Ghana.

A recent review by Speakman *et al.* (2014) reported that "The (reviewed) papers show that LUTS are common in the UK, affecting ≈3% of men aged 45-49 years, rising to >30% in men aged ≥85 years". The prevalence of LUTS suggestive of BPH (especially in older men) is clearly high globally. Studies that definitively diagnosed BPH, especially in hospitalised patients, however report lower values. For instance, in the US, among hospitalized patients, the age-adjusted prevalence of BPH has been reported to have increased from 4.3% in 1998 to 8% in 2008
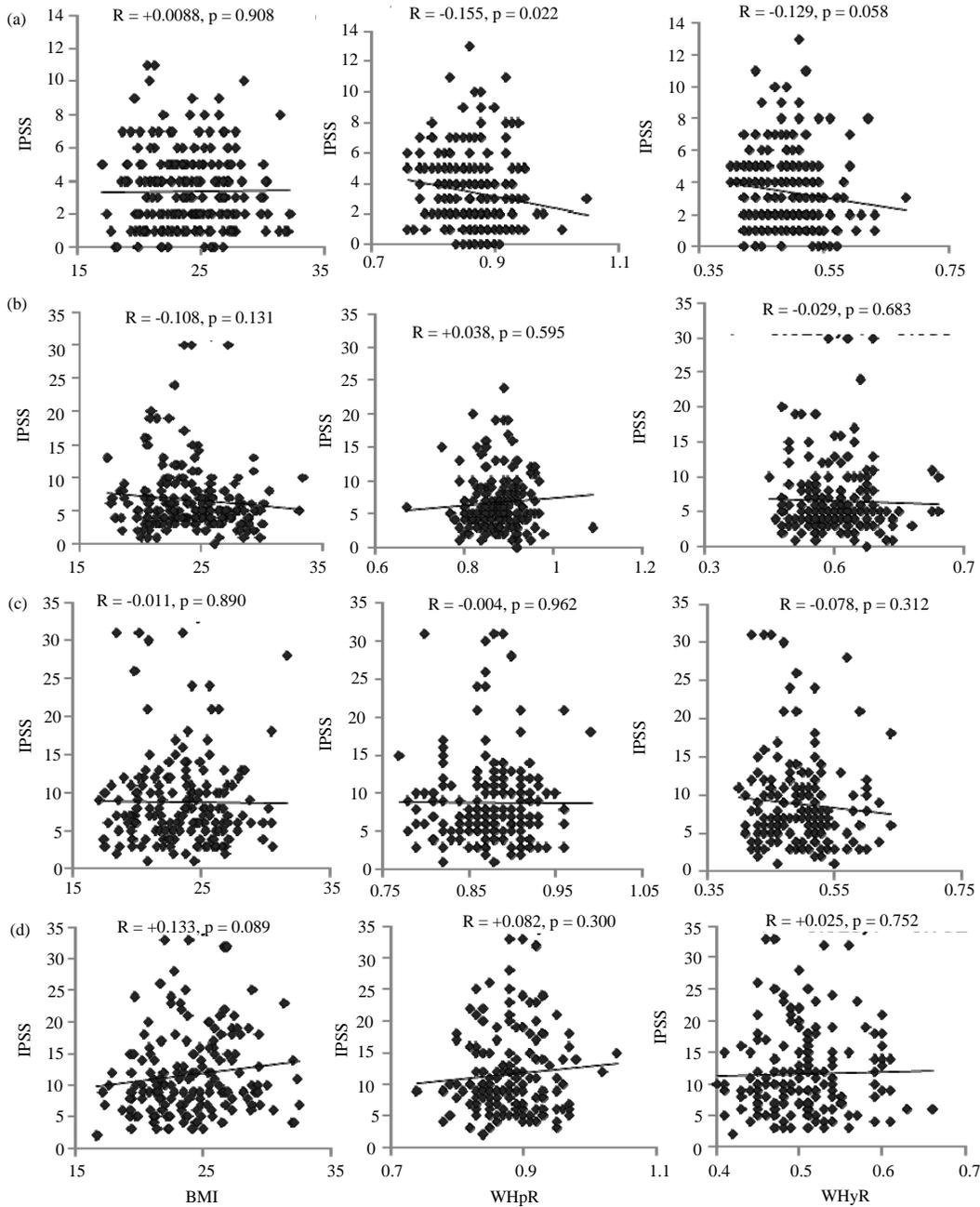
Fig. 1(a-d): Correlations between International Prostate Symptom Scores (IPSS) and measures of obesity in the studied population, a, b, c and d represent data for those aged 40-49, 50-59, 60-69 and 70+years, respectively

(Stroup *et al.*, 2012). Differences in sample characteristics and diagnostic methodologies however, foreclose any objective comparison between most of available literature on the prevalence of BPH. The values for the measures of obesity (except for WHpR between those with moderate vs mild symptoms, in the general population) were statistically similar (p>0.05) between the symptom score

5

groups. Furthermore, no strong significant correlation was found between prostate symptom scores and measures of obesity. Regression analyses showed that only WHpR was associated with symptom scores and even that was weak (β = +0.099) while, the models accounted for only 0.2-0.5% of the data. Our data therefore, suggest that general obesity may be minimally associated with the clinical symptoms of BPH.

This finding of a lack of association between BMI and clinical symptoms of BPH is not an isolated case. Haidinger *et al.* (2000) after studying 1500 men in Australia showed that IPSS and waist circumference (but not BMI) were linearly correlated. Dahle *et al.* (2002) studied 502 Chinese men and reported no significant relationship between BMI and BPH/LUTS. The said authors however showed that individuals with a WHpR in the highest quartile (compared to those in the lowest quartile) had a significant 2.0-fold higher risk of developing symptomatic BPH. Joseph *et al.* (2003) and Wong *et al.* (2006) also independently reported a lack of association between obesity determined by BMI and LUTS in black American men and in Chinese men, respectively. The absence of association between BMI, WHtR on the one hand and BPH on the other hand, in this study, may be due to the fact that the studied population had very few obese individuals. The same challenge was reported by Dahle *et al.* (2002).

Though the studied population is considerably lean, the WHpR showed some promise, albeit modestly, as an independent predictor of BPH. This is probably because the problem with obesity for which it is linked to BPH is, in fact, excess (visceral) adiposity. Unfortunately, both BMI and WHtR falsely distribute the excess weight throughout the entire body due to the formulae used to derive them, such that BMI (in particular) is sometimes erroneously linked to morbidity and mortality (Gallagher *et al.*, 2000). Contrariwise, it is possible to be obese by BMI standards and yet post a healthy metabolic profile (Ejike *et al.*, 2009). The WHpR, unlike BMI and WHtR measures obesity, where it matters with respect to BPH. In fact, WHpR is known to predict obesity-related health risks better than BMI (Gharakhanlou *et al.*, 2012). These may explain the association observed between WHpR and LUTS/BPH (albeit a weak one) and a lack of such association between BMI, WHtR and the symptoms.

Seim *et al.* (2005) after examining the data of 21,694 Norwegian males reported that both BMI and WHpR significantly predicted moderate to severe LUTS. The said authors defined LUTS using the IPSS as used in this study. It is therefore, interesting that our data is in concordance with theirs on WHpR but not BMI. The larger sample size in their study, implicit in which is a larger number of obese subjects, other than genetic and the environmental factors may explain the differences. Kristal *et al.* (2007) had shown that a 0.05 increase in WHpR increased the severity of symptoms and incidence of BPH by as much as 10%. There may therefore, be merit in investigating the association between WHpR and LUTS/BPH in a larger population of Nigerian males.

Contrary to our findings, Parsons *et al.* (2006) observed that men with BMI ≥ 35 kg m^{-2} (compared to those with a BMI 25 kg m^{-2}) had a 3.5-fold higher risk of bearing an enlarged prostate. There are several other studies in the literature reporting an association between BMI and BPH. Some other studies are apparently equivocal about that relationship (Zucchetto *et al.*, 2005), while others report no links between obesity and BPH (Gupta *et al.*, 2006; Fritschi *et al.*, 2007). Again, methodological differences make comparisons extremely difficult. Yet, one must observe that smaller studies were more likely to show no association between obesity and BPH, whereas, larger studies more often show an association between the two. From the data presented in this report, visceral obesity may be more important than generalised obesity with respect to relationship with BPH.

This study is limited by our inability to definitively diagnose BPH in our subjects. This was warranted by the unavailability of the needed equipment and skill and the lack of funds to finance such an elaborate study. The IPSS used here is however, known to be valid for use for the diagnosis of LUTS/BPH (Ezeanyika *et al.*, 2006; Roehrborn *et al.*, 2008; Amu *et al.*, 2013). The data presented here, therefore represent an important starting point in the investigation of the relationship between modifiable risk factors and prostatic diseases. This study would have benefitted from being more nationally representative and including data on the food/nutrient consumption of the subjects. However, that would have required massive funding which is currently not available. We nonetheless, hope that this would help in highlighting the problems of men's health and therefore stimulate funding for such research.

CONCLUSION

In conclusion, this study investigated the prevalence of symptoms of BPH and the relationship between such symptoms and measures of obesity in a population of adult male Nigerians, in Umudike, Abia State. The prevalence of LUTS suggestive of BPH (moderate-to-severe symptoms) in the said population is 35.3% (6.0% in those aged 40-49 years to 69.9% in those aged 70+ years). Only WHpR, but not BMI nor WHtR, was found to be minimally associated with symptoms of BPH. It appears that visceral adiposity may be the critical part of obesity that is related to BPH. A larger more nationally representative study, which will target more obese people, is warranted.

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